

REMARKS

Claims 32 to 34 and 41 to 43 have been canceled without prejudice or disclaimer. Claims 30, 31, 39, and 40 have been amended. The specification has been amended to provide a brief description of new figures. The attached Appendix shows the changes to the specification and the claims. Claims 30, 31, 35 to 40, and 44 to 47 are pending and under consideration.

Claims 30 and 39 were amended to include the language "fluorescence optical signal", which was previously included in dependent claims 34 and 43. Claims 30 and 39 further were amended to include the language "while the amplification reaction is in progress and without opening the at least one reaction vessel." That language is supported in the specification, e.g., at page 6, lines 22 to 23, and line 27. That reworded language is intended to make claims 30 and 39 easier to read. Dependent claim 31 was amended to delete language that was redundant in view of claim 30. Dependent claim 40 was amended to change the word "instrument" to the word "system" to track the language of the claim 39. Dependent claim 45 was amended to add the words "at least one" before the word "vessel" to track the language of the amended claim 39.

Applicants thank Examiner Snay for the personal interview with the undersigned and Mr. Charles Van Horn on July 22, 2002. The following remarks reflect and expand upon the discussion during the interview.

I. Objection To The Drawings Under 37 C.F.R. § 1.83(a)

The Examiner objected to the drawings because they allegedly fail to show the detail of the apparatus as described in the specification. Office Action at page 2, Item 1.

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The Examiner objected to the drawings because they allegedly fail to show every feature of the invention in the claims. *Id.* at page 2, Item 2.

During the interview the Examiner agreed that all of the drawing objections in the Action were based on the requirement to provide a drawing of sufficient detail whenever the nature of the subject matter sought to be patented admits of illustration by a drawing without its being necessary for the understanding of the subject matter. The Examiner agreed that drawings were not required in order to receive a filing date with respect to the apparatus claims.

Above, applicant requests that the drawings be amended by replacing the drawings submitted in the amendment that was filed February 26, 2002 (February 2002 Amendment) (Figures 6A and 6B), with the new Figures 6A, 6B, 7, and 8. Applicant respectfully asserts that the new figures adequately illustrate all of the presently claimed features that the Examiner listed at pages 2 and 3 of the Action. Each of those features will now be discussed.

A. Item 1 Of The Action

The Examiner contended that more structural detail was needed with respect to: (1) a fluorometer for detection of fluorescence emission from each of a plurality of reaction tubes; (2) reaction vessels being "light sealed", e.g., by a clear or translucent cap; and (3) a light source and an optical system that "moves the excitation light from the source to the reaction tube." Action at page 2, Item 1.

Applicant respectfully submits that the Examiner's remarks are misplaced inasmuch as Items 2 and 3 are drawn from the specification, not the claims. Applicant is unaware of any requirement that all structures described in the specification must also appear in the drawings. Rather, drawing requirements relate to the claims.

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As asserted in the February 2002 Amendment, under Rule 83(a), "conventional features disclosed in the description and claims, where their detailed illustration is not essential for a proper understanding of the invention, should be illustrated in the drawing in the form of a graphical drawing symbol or a labeled representation (e.g., a labeled rectangular box)."

First, New Figure 6B schematically shows a detector operable to detect signal from a plurality of reaction vessels. Under Rule 83(a), no further detail is required since it is clear to one skilled in the art that any suitable detector configuration could be used. The specification discusses certain exemplary detectors at pages 14 and 15. As a nonlimiting example, the specification teaches that the fluorescence could be read using an apparatus similar to an ELISA plate reader, as illustrated by a Cytofluor™ 2300 machine manufactured by Millipore (page 15, first full paragraph), which could read fluorescence signals from multiple wells of a microtiter plate.

Accordingly, detectors that were operable to detect a fluorescent optical signal from a plurality of reaction vessels were known in the art when this application was initially filed. Thus, further detail than that provided in Figure 6B is not needed for compliance with Rule 83(a) for such embodiments.

Second, new Figure 7 schematically shows certain embodiments according to claim 45, which recites that the at least one reaction vessel includes a clear or translucent cap. Under Rule 83(a), no further detail is required with respect to such embodiments.

Third, claims 30 and 39 do not recite the language "an optical system that moves the excitation light from the source to the reaction tube." In fact, those claims have been amended to change the language "optical system including a detector" to "a detector". Thus, although certain embodiments of the claimed invention may be used

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with a device that provides excitation light, such a feature is not recited in the claim language. Accordingly, there is no requirement to include such a feature in the drawings.

B. Item 2 Of The Action

At Item 2 of the Action, the Examiner listed additional features that allegedly need to be included in drawings. Each of those features is now discussed.

First, the Examiner contended that the drawings must show the structural relationship between the optical system and the thermal cycler such that the detector is "operable to detect an optical signal . . . with the reaction vessel in a sealed condition" (Item 2 (a)). During the interview, applicant's representatives stated that thermal cyclers and detectors were known in the art at the time the present application was initially filed. As discussed at the interview, the Examiner has not explained why one skilled in the art would need further structural detail in order to understand this aspect of the invention. Specifically, the Examiner has not established that one skilled in the art, in view of the present specification, would require more detailed structural illustration to understand the structure of an instrument or system employing a thermal cycler and "a detector operable to detect a fluorescence optical signal while the amplification reaction is in progress and without opening the at least one reaction vessel"

Further detail than that provided in Figures 6A and 6B is simply not required to illustrate such an instrument or system. In fact, in situations in which conventional elements such as thermal cyclers and detectors are employed, Rule 83(a) permits schematic drawings such as labeled boxes. Accordingly, new Figures 6A and 6B satisfy the drawing requirements with respect to a thermal cycler and detector according to the claims.

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Second, the Examiner contended that the drawings must show a reaction vessel in a sealed condition (Item 2(b)). As discussed above with respect to Item 1, new Figure 7 schematically shows certain embodiments according to claim 45, which recites that the at least one reaction vessel includes a clear or translucent cap.

Third, the Examiner contended that the drawings must show a sealed transmission path (Item 2(c)) and a fiber optic cable (Item 2d). Applicants have proposed adding new Figure 7, which illustrates certain embodiments of the invention that employ a sealed transmission path, such as a fiber optic cable. Support for Figure 7 is found in the specification, e.g., at page 14, third paragraph, and at the paragraph bridging pages 28 and 29.

Fourth, the Examiner contended that the drawings must show a computer controller (Item 2(e)). Applicants have proposed adding new Figure 8, which illustrates certain embodiments of the invention that employ a computer controller. Support for Figure 8 is found in the specification, e.g., at page 11, at the paragraph beginning on line 19. In that paragraph, EP No. 236,069 (EP '069) is incorporated by reference. EP '069 discloses a computer controller used with a thermal cycler. See EP '069, e.g., at the abstract on the cover page and at page 3.¹ EP '069 shows that it was conventional to design a thermal cycler that is computer-controlled, and thus, further detail than that provided in Figure 8 is not needed to comply with Rule 83(a).

Fifth, the Examiner contended that the drawings must show a reaction vessel including a clear or translucent cap optically coupled to the detector by a sealed light transmission path (Item 2(f)). Applicants have proposed adding new Figure 7, which illustrates certain embodiments of the invention that employ a clear or translucent cap

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¹ A copy of EP '069 is enclosed. EP '069 substantially corresponds to US Patent No. 5,038,852.

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optically coupled to the detector by a sealed light transmission path. Support for Figure 7 is discussed above.

Applicants request reconsideration and withdrawal of the objection to the drawings.

II. Rejections Under 35 U.S.C. § 112, First Paragraph

A. Enablement Rejections

First, the Examiner rejected claims 30 to 33, 36 to 42, and 45 to 47 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification. Action at page 3, Item 4. Specifically, the Examiner stated that the claims were enabled for a fluorescence detector, but were not enabled for any other "optical system" to "detect an optical signal related to the amount of amplified nucleic acid." *Id.*

Applicants respectfully traverse the rejection. The burden is on the Examiner to establish that one skilled in the art would require undue experimentation to practice the claimed invention. In the current rejection, the Examiner fails to even make such a conclusion, let alone provide evidence supporting it.

Furthermore, the rejection is moot in view of amended claims 30 and 39, which incorporate certain language from canceled 34 and 43, respectively (fluorescence optical signal). The current rejection under § 112, first paragraph, was not asserted against claims 34 and 43. Applicants reserve the right to pursue claims directed to other detectors in a related application. Accordingly, reconsideration and withdrawal of this § 112, first paragraph, enablement rejection is requested.

Second, the Examiner rejected claims 30 to 47 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification. Action at page 4, Item 5. Specifically, the Examiner stated that "[t]he use of the apparatus in which elements

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are critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure." *Id.* The Examiner considered that "an excitation light source, optical communication means between the thermal cycler and detector, and reaction vessels [were all] essential elements in the use of the claimed apparatus for monitoring a nucleic acid amplification reaction." *Id.*² Applicant respectfully traverses the rejection.

The Examiner fails to support his position that claims directed to an apparatus must recite all elements needed for an apparatus to function. For example, certainly a claim directed to an improvement in a car engine need not recite every element of the car engine that may contribute to the engine's overall function. Moreover, a claim directed to a microscope need not recite the microscope slide that is used to observe a sample. Likewise, the current claims need not recite an excitation light source, an optical communication means, and reaction vessels.

Moreover, claims 30 and 39 have been amended to recite that the instrument (claim 30) and the system (claim 39) are "for use in monitoring a nucleic acid amplification reaction" Thus, those claims are clearly directed to a subcombination of elements for use in monitoring, and other elements that may be employed in such monitoring clearly need not be recited in the claims.

For these reasons, reconsideration and withdrawal of this § 112, first paragraph, enablement rejection is requested.

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² The Examiner also contended that the extent of the specification that is available for support and enablement of the claimed apparatus is limited to the disclosure at page 14, line 1, to page 15, line 6, and at page 28, line 25, to page 29, line 9. Applicant disagrees with that contention. If it is maintained, applicants respectfully request that the Examiner explain why other text in the specification is not available.

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B. Written Description Rejection

The Examiner rejected claims 30 to 47 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention. Action at pages 4 to 5, Item 6. Applicant traverses the rejection.

First, the Examiner contended that "the specification fails to describe how any excitation light source would have been constructed and coordinated with a detector to operate as claimed." *Id.* at page 5. Further, the Examiner contends that "[t]he specification contains no description of detecting a signal over a multiple cycle period." *Id.*

The Examiner has not met his burden of establishing a failure to satisfy the written description requirement. First, the written description requirement is applied to the language of the claims. The Examiner's focus on an excitation light source is misplaced because there is no such language in any of the rejected claims.

Even if such language were included in the claims, however, the specification would have conveyed to one skilled in the art that applicant was in possession of such a feature. Moreover, the specification provides description of a detector operable to detect a fluorescence optical signal while the amplification reaction is in progress. Specifically, the specification clearly conveys possession of an instrument or system that includes an optical system that provides excitation light and detects fluorescence during an amplification reaction. See the specification, e.g., at pages 14 and 15. The Examiner fails to explain why that disclosure would not have conveyed possession of such an optical system or detector to one skilled in the art. Moreover, a particular nonlimiting embodiment is set forth in Example VIII at pages 28 to 29.

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Accordingly, the Examiner did not establish a failure to satisfy the written description requirement with respect to this first basis.

Second, the Examiner contended that "[t]he specification further fails to describe and support the claimed feature of the detector to 'distinguish the detected signal from any other optical signals originating in the reaction vessel.'" Action at page 5. This basis for the rejection is moot in view of the cancellation of claims 33 and 42.

Third, the Examiner contended that "[t]he specification further fails to describe the presently recited feature of the thermal cycler being computer-controlled." Action at page 5.

As discussed above in the section dealing with the drawing objections, the present specification incorporates by reference EP '236, which discloses a thermal cycler that is computer-controlled. See EP '236, e.g., at the abstract on the cover page and at page 3. Figure 8 has been added to schematically show a thermal cycler that is computer-controlled. Accordingly, the third basis for the rejection is moot.

Applicants respectfully request reconsideration and withdrawal of this § 112, first paragraph, written description rejection.

III. Rejection Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 30 to 38 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Action at page 5, Item 8. Specifically, the Examiner contended that "the system is operable to detect a signal while the reaction vessel is in a sealed condition, which is clearly dependent upon the particular reaction vessel." *Id.* The Examiner then contends that the claim is of indeterminate scope unless the reaction vessel is recited as a structural element of the claim. *Id.* Applicant respectfully traverses this rejection.

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To maintain a rejection based on indefiniteness under § 112, second paragraph, the Examiner must establish that one skilled in the art would not understand what is encompassed by the claim in view of the specification. Amended claim 30 recites "a detector operable to detect a fluorescence optical signal while the amplification reaction is in progress and without opening the at least one reaction vessel." The Examiner has not explained why one skilled in the art would not understand what is encompassed by such a detector. The claim need not include the vessel as a structural limitation for one skilled in the art to understand what is encompassed by the detector as claimed in claim 30.

A simple analogy may be useful. Assume that a claim recites "a microscope comprising: . . . a platform adapted to receive a microscope slide, and a light source operable to emit light through the microscope slide." The claim term "light source" should not be found indefinite under § 112, second paragraph, if the claim does not positively recite the microscope slide as a structural element.

Thus, applicant respectfully requests reconsideration and withdrawal of the § 112, second paragraph, rejection.

IV. Rejection Under 35 U.S.C. § 103

The Examiner rejected claims 30 to 47 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Haff (*Amplifications*, 1:8-10 (1989)) in view of Mackay (EP 0266881) and Schnipelsky (US Patent No. 5,229,297). See Action at page 6. The Examiner referred to a prior Office Action for the reasons for the rejection and then discussed applicant's arguments that were included in the amendment that was filed February 26, 2002. See *id.* at pages 6 to 7.

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Applicant respectfully traverses the rejection. Rather than repeat all of the prior arguments, applicant incorporates by reference all of the prior arguments presented in the February 2002 Amendment. During the interview, applicant's representatives summarized prior arguments. The Examiner agreed that the rejection over the art of record would be withdrawn if the claims more clearly recited that the detector was operable to detect during the amplification reaction, in contrast to a detector that was not operable during an amplification reaction.

Applicant submits that the § 103 rejection is moot in view of amended claims 30 and 39, which recite "a detector operable to detect a fluorescence optical signal while the amplification reaction is in progress and without opening the at least one reaction vessel, which fluorescence optical signal is related to the amount of amplified nucleic acid in the reaction vessel." Accordingly, applicant respectfully requests reconsideration and withdrawal of the § 103 rejection.

Applicant respectfully asserts that the application is in condition for allowance and requests issuance of a Notice of Allowance. If the Examiner does not consider the application to be in condition for allowance, applicant requests that he call the undersigned at (650) 849-6620 to set up an interview.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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By: 

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Dated: August 22, 2002

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APPENDIX

IN THE SPECIFICATION:

Replacement for the paragraph inserted at page 6, line 17, in the amendment submitted February 11, 2000, with the following three paragraphs:

[Figures 6A and 6B are schematic illustrations of a thermal cycler having one (Fig. 6A) or a plurality of reaction vessels (Fig. 6B), and an optical system, constructed in accordance with embodiments of the invention.]

Figures 6A and 6B schematically show a detector and a thermal cycler according to certain embodiments of the invention.

Figure 7 schematically shows certain embodiments of the invention that employ a fiber optic cable.

Figure 8 schematically shows certain embodiments of the invention in which a thermal cycler is computer-controlled.

IN THE CLAIMS:

30. (Amended) An instrument for use in monitoring a nucleic acid amplification reaction [over] comprising multiple thermal cycles, comprising:

(a) a thermal cycler capable of alternately heating and cooling, and adapted to receive, [a] at least one reaction vessel containing an amplification reaction mixture comprising a target nucleic acid, reagents for nucleic acid amplification, and a detectable nucleic acid binding agent[, in a sealed reaction vessel condition]; and

(b) [an optical system including] a detector operable to detect [an] a fluorescence optical signal while the amplification reaction is in progress and without

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opening the at least one reaction vessel, which fluorescence optical signal is related to the amount of amplified nucleic acid in the reaction vessel [over a multiple-cycle period, with the reaction vessel in a sealed condition, allowing determination of a cycle-dependent change in such optical signal over a multiple-cycle period with the reaction vessel in its sealed condition].

31. (Amended) The instrument of claim 30, wherein the thermal cycler is [capable of alternately heating and cooling, and] adapted to receive[,] a plurality of reaction vessels, each containing an amplification reaction mixture.

39. (Amended) A system for use in monitoring a nucleic acid amplification reaction [over] comprising multiple thermal cycles, comprising:

(a) [a] at least one reaction vessel adapted to contain an amplification reaction mixture comprising a target nucleic acid, reagents for nucleic acid amplification, and a detectable nucleic acid binding agent[, in a sealed reaction vessel condition];

(b) a thermal cycler capable of alternately heating and cooling such a reaction vessel, and

(c) [an optical system including] a detector operable to detect [an] a fluorescence optical signal while the amplification reaction is in progress and without opening the at least one reaction vessel, which fluorescence optical signal is related to the amount of amplified nucleic acid in the reaction vessel [over a multiple-cycle period, with the reaction vessel in a sealed condition, allowing determination of a cycle-

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d pendent change in such optical signal over a multiple-cycle period with the reaction vessel in its sealed condition].

40. (Amended) The system of claim 39, wherein the [instrument] system comprises a plurality of reaction vessels, each adapted to contain an amplification reaction mixture.

45. (Amended) The system of claim 39, wherein the at least one reaction vessel includes a clear or translucent cap optically coupled to the detector by a sealed light transmission path.

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